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Raghu

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Rajagopalan, et al.
Serial No.: 09/898,885
Filed: July 3, 2001
Group Art Unit: 1641
Confirmation No: 2179
Examiner: Ceperley, Mary
Title: **DYE-AZIDE COMPOUNDS FOR DUAL PHOTOTHERAPY**
Our Ref. No.: MRD-62

Cincinnati, Ohio 45202

April 11, 2003

Assistant Commissioner for Patents
Washington, D.C. 20231

DECLARATION OF RAGHAVAN RAJAGOPALAN
PURSUANT TO 37 C.F.R. §1.132

Sir:

I, RAGHAVAN RAJAGOPALAN, declare as follows:

1. I am an inventor in the above-identified patent application.
2. I hold a Ph.D. in Organic Chemistry from Columbia University. I have 20 years of experience in the synthesis and use of compounds for medical diagnosis and therapy, which is the subject of the application. I have read the outstanding Office Action and understand the position of the Examiner.

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3. In my opinion, none of the references cited, namely, none of Pochinok, Ol'shevskaya, Clecak, and Leung disclose my invention because none disclose the dye-azide compound in a pharmaceutically acceptable formulation.

4. One skilled in the art would appreciate that a "pharmaceutically acceptable formulation" is one that is to be administered to an animal or human with an optimal bioavailability of the dye-azide *in vivo*, maximal chemical and physical stability *in vitro* or *in vivo*, and on the technical feasibility of producing the formulation containing the dye-azide compound.

5. It is further my opinion that the "solvents" in the "compositions" for the dye compounds used by Leung et al. (DMSO and "lower alcohol or other completely water miscible solvent"), Clecak (ethanol), Pochinok ("dyes in solution"), and Ol'shevskaya (ethanol solution), address only the technical feasibility of producing the formulation without addressing the bioavailability or the chemical and physical stability. Because all parameters must be considered, it is my opinion that none of the references disclose the invention.

6. Bioavailability is a pharmacokinetic parameter that represents the degree of availability to produce a pharmacological action. Chemical and physical stability, and bioavailability, effect the other: for example, a decreased bioavailability may result from a poorly formulated dose that fails to dissolve in body fluids, interactions between the dye-azide and other drugs, metabolism of the dye-azide, and so on. Bioavailability

depends upon absorption, distribution, biotransformation, and excretion, one or more of which may depend upon the patient's physical and/or physiological state, body mass, age, gender, etc.

7. These solvents, as described in the cited references, are for *in vitro* procedures and there is no disclosure of the compositions for the *in vivo* administration to an animal or human of an active compound in a "pharmaceutically acceptable formulation".

8. For the above reasons, I respectfully assert that the dye compounds in the prior art do not anticipate the formulation of claim 40.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the subject application or any patent issued thereon.

April 11, 2003
Date

Raghavan Rajagopalan
Raghavan Rajagopalan, Ph.D.